ATTORNEY DOCKET NO. CFBF-P02-004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Denisa D. Wagner, et al. Examiner:

Serial No.: Art Unit:

Filing Date:

For: METHOD FOR TREATING AND PREVENTING ATHEROSCLEROSIS

Express Mail Label No. EL 920 873 421 US
Date of Deposit: 6\18\01

I hereby certify that this Application for a Continuation Application is being deposited with the United States Postal Service as Express Mail on the date indicated above and is addressed to: Commissioner for Patents, Attention Box Continuation Application, Washington, DC 20231.

Name: Nathan Denny

COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

Dear Sir:

PRELIMINARY AMENDMENT

Please amend the above-identified application prior to examination as follows:

IN THE SPECIFICATION:

Please insert the following section on Page 1, line 1 of the specification immediately following the Title of the invention---

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of application serial no. 09/436,076, filed November 8, 1999, which is a continuation of application serial no. 08/948,393, filed October 10, 1997, now abandoned, which is a continuation of application serial no. 08/377,798, filed January 24, 1995, now abandoned, which is a continuation-in-part of application serial no. 08/253,663, filed May 3, 1994, now abandoned.---

IN THE CLAIMS:

Please cancel claims 1-38 without prejudice.

Please add the following new claims:

39. A method for treating or inhibiting atherosclerosis in a mammal, comprising:

providing an agent for inhibiting an interaction between P-selectin and a ligand of P-selectin, and between E-selectin and a ligand of E-selectin; and

administering said agent to a mammal in need of such treatment so as to cause such inhibition to occur, wherein said agent is selected from the group consisting of an inhibitory protein, an inhibitory peptide, an inhibitory carbohydrate, an inhibitory antibody, an inhibitory sulfatide, a substance obtained form a snake venom a plant extract, and an inhibitor of granular release.

40. The method of claim 39 wherein said agent is administered to the mammal in conjunction with a vessel-corrective technique.

41. The method of claim 40 wherein the vessel corrective technique is selected from the group consisting of angioplasty, a stenting procedure, atherectomy, and bypass surgery.

42. The method of claim 39 wherein said P-selectin is on a cell.

43. The method of claim 39 wherein said cell is an endothelial cell.

44. The method of claim 42 wherein said cell is a platelet.

45. The method of claim 39 wherein said E-selectin is on an endothelial cell.

46. The method of claim 39 wherein said ligand of P-selectin comprises a carbohydrate.

47. The method of claim 39 wherein said ligand of P-selectin comprises a glycoprotein.

48. The method of claim 39 wherein said ligand of P-selectin is selected from the group consisting of sialyl-Lewis x, sialyl-Lewis a, sialyl-Lewis x-pentasaccharide, polyactosaminoglycan, carbohydrate containing 2,6 sialic acid, Lewis x 3'-0-sulfate, heparin oligosaccharides, PSGL-1, 160 kD monospecific P-selectin ligand and lysosomal membrane glycoproteins.

49. The method of claim 39 wherein said ligand of P-selectin is on a cell selected from the group consisting of monocytes, neutrophils, eosinophils, CD4+ T cells, CD8+ T cells, and natural killer cells.

50. The method of claim 39 wherein said ligand of P-selectin is on a leukocyte.

51. The method of claim 50 wherein said leukocyte is a neutrophil.

52. The method of claim 50 wherein said leukocyte is a monocyte.

53. The method of claim 39 wherein said agent is selected from the group consisting of a soluble form of at least a fragment of said P-selectin and a soluble form of at least a fragment of said ligand of P-selectin.

54. The method of claim 39 wherein said agent is an inhibitory carbohydrate.

55. The method of claim 54 wherein said inhibitory carbohydrate is selected from the group consisting of sialyl-Lewis x and its analogs, sialyl Lewis a and its analogs, and carbohydrates containing 2,6 sialic acid.

56. The method of claim 39 wherein said agent is an inhibitory sulfatide.

57. The method of claim 39 wherein said agent is an inhibitory antibody to P-selectin or P-selectin ligand.

58. The method of claim 39 wherein said agent is selected from the group consisting of an analog of said P-selectin and an analog of said ligand of P-selectin.

59. The method of claim 39 wherein said agent is obtained from snake venom or a plant extract.

60. The method of claim 39 wherein said agent is an inhibitor of granular release.

61. The method of claim 39 wherein said agent is an inhibitor of a molecule required for the synthesis, post-translational modification or functioning of said P-selectin or said ligand of P-selectin.

62. The method of claim 39 wherein said agent inhibits interaction between said P-selectin and said ligand of P-selectin or between said E-selectin and said ligand of E-selectin so as to at least partially inhibit formation of an atherosclerotic fatty streak, or a least partially reverse a formed atherosclerotic fatty streak.

63. The method of claim 39 wherein said agent inhibits interaction between said P-selectin and said ligand of P-selectin or between said E-selectin and said ligand of E-selectin so as to at least partially prevent formation of an atherosclerotic intermediate lesion, or at least partially reverse a formed atherosclerotic intermediate lesion.

64. The method of claim 39 wherein said agent inhibits interaction between said P-selectin and said ligand of P-selectin or between said E-selectin and said ligand of E-selectin so as to at least partially inhibit formation of an atherosclerotic fibrous plaque, or at least partially reverse a formed atherosclerotic fibrous plaque.

65. The method of claim 39 wherein said agent inhibits interaction between said P-selectin and said ligand of P-selectin or between said E-selectin and said ligand of E-selectin so as to at least partially prevent growth of an atherosclerotic lesion after a surgical procedure for at least partially inhibiting restinosis.

66. The method of claim 39 wherein said administering occurs prior to formation of an atherosclerotic lesion.

67. The method of claim 39 wherein said administering occurs subsequent to formation of an atheroschlerotic lesion.

68. The method of claim 39 wherein said mammal is a human.

69. A therapeutic agent in a dosage form and concentration suitable for treating or inhibiting atheroschlerosis in a mammal in need of such treatment, said agent being effective to inhibit interaction between P-selectin and a ligand of P-selectin or between E-selectin and a ligand of E-selectin, wherein said therapeutic agent is selected from the group consisting of an inhibitory protein, an inhibitory peptide, an inhibitory carbohydrate, an inhibitory antibody, an inhibitory sulfatide, a substance obtained from a snake venom or a plant extract, and an inhibitor of granular release.

70. The method of claim 39, wherein said inhibitory carbohydrate is a heparin oligosaccharide.

71. The method claim 39, wherein said agent is administered at a dose of about 0.01 to about 200 mg/kg body weight.

72. The method of claim 69, wherein said agent is administered at a dose of about 1 to about 100 mg/kg body weight.

73. The method of claim 39, wherein said agent further inhibits interaction between L-selectin and a ligand of L-selectin.

74. A method for treating or inhibiting atherosclerosis in a mammal, comprising:

providing an agent for inhibiting interaction between P-selectin and a ligand of P-selectin and between L-selectin and a ligand of L-selectin; and

administering said agent to a mammal in need of such treatment so as to cause such inhibition to occur.

75. The method of claim 39, wherein said P-selectin ligand is PSGL-1 or a fragment thereof.

76. The method of claim 39, wherein said agent is administered in sequential exposures over a period of hours, days, weeks, months or years.

77. The method of claim 39, wherein said agent is administered repeatedly, or by a controlled release delivery system.

78. The method of claim 39, wherein said agent is administered in combination with other therapeutic agents.

79. The method of claim 39, wherein the agent is administered as a pill, as an injection or as an implant.

80. A method for treating or inhibiting atherosclerosis in a mammal comprising:

providing an agent for inhibiting an interaction between P-selectin and a ligand of P-selectin and between E-selectin and a ligand of E-selectin; and

administering said agent to a mammal in need of such treatment so as to cause such inhibition to occur, wherein said agent is a mimetic of an inhibitory carbohydrate of P-selectin or the ligand of P-selectin.

81. A method for treating or preventing restenosis in a mammal, comprising:

providing a method for inhibiting an interaction between P-selectin and a ligand of P-selectin, or between E-selectin and a ligand of E-selectin; and

administering an effective amount of said agent to a mammal in need of such treatment so as to cause such inhibition to occur, wherein said agent is selected from the group consisting of an inhibitory protein, an inhibitory peptide, an inhibitory carbohydrate, an inhibitory antibody, an inhibitory sulfatide, a substance obtained form a snake venom a plant extract, and an inhibitor of granular release, said agent being administered in conjunction with or after a vessel-corrective technique.

82. The method of claim 81, wherein said vessel-corrective technique is selected form the group consisting of angioplasty, stenting procedure, atherectomy, and bypass surgery.

83. The method of claim 81, wherein said agent comprises a soluble form of a P-selectin ligand or a fragment thereof.

84. The method of claim 81, wherein said agent is administered in sequential exposures over a period of hours, days, weeks months or years.

85. The method of claim 81, wherein said agent is administered in combination with other therapeutic agents.

86. The method of claim 81, wherein said P-selectin ligand is PSGL-1 or a fragment thereof.

87. The method of claim 81, wherein said agent is a mimetic of an inhibitory carbohydrate of P-selectin or the ligand of P-selectin.

88. A method for treating or inhibiting atherosclerosis in a mammal comprising:

providing an agent for inhibiting an interaction between P-selectin and a ligand of P-selectin; and

administering said agent to a mammal in need of such treatment so as to cause such inhibition to occur, wherein said agent is selected from the group consisting of an inhibitory protein, an inhibitory peptide, an inhibitory carbohydrate, an inhibitory antibody, an inhibitory sulfatide, a substance obtained form a snake venom a plant extract, and an inhibitor of granular release.

REMARKS

The claims of this application have now been amended to cancel the claims as originally files, and to present a new set of claims. The new claims are fully supported by the specification and are deemed to be patentable over the prior art applicant is aware of. These new claims are being submitted at this time to facilitate the Examiner's consideration of this application.

Accordingly, early and favorable action on this application is solicited.

Respectfully submitted,

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